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C−H Functionalization of 1,4-Naphthoquinone by Oxidative Coupling with Anilines in the Presence of a Catalytic Quantity of Copper(II) Acetate

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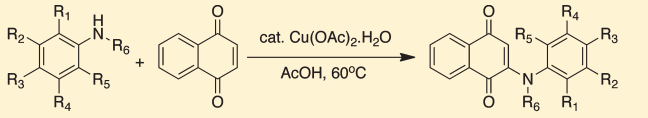
Supporting Information

ABSTRACT: The oxidative addition of anilines (**2**) with 1,4-naphthoquinone (**3**) to give *N*-aryl-2-amino-1,4-naphthoquinones (**1**) was found to be catalyzed by copper(II) acetate. In the absence of the catalyst, the reactions are slower and give lower yields with the formation of many colateral products. In the presence of 10 mol % hydrated copper(II) acetate, the reactions are generally more efficient in that they are cleaner, higher yielding, and faster.



$R_{1\text{-}5}$ = F, Cl, Br, I, Me, NH_2, OMe, CN, CO_2H, NO_2, CF_3; R_6 = H, Me: good to excellent yields

INTRODUCTION

The 2-amino-1,4-napthoquinone (**1**) moiety and the related quinoline- and isoquinoline- 5,8-diones (azanaphthoquinones) are found in a considerable number of natural product antibiotics (Figure 1). The structures of these compounds are very diverse possessing 2−5 fused rings, for example, cribrostatins;[1] lavendamycin[2] and streptonigrin;[3] renierones;[4] mimosamycin;[5] caulibugulones A−F;[6] mansouramycins A−D, recently isolated from the marine-derived *Streptomyces* sp. isolate Mei37;[7] hygrocins A and B, isolated during the purification of the immunosuppressive agent rapamycin from *Streptomyces hygroscopicus* ATC25293;[8] benzo[*b*]phenanthridines, a subgroup of the angucycline antibiotics,[9] such as the jadomycins[10] and phenanthroviridone;[11] griffithazanone A and the azaanthracenetrione, isolated from the ethanolic extract of the roots of *G. griffithii*;[12] and the more complex pentacyclic systems of jorunnamycin,[13] renieramycins[14] and the saframycins.[14a,15] Very significant cytotoxicity has been observed for the aforementioned natural products.

The reaction of amines and anilines (**2**) with 1,4-naphthoquinone (**3**) to give 2-amino- and 2-anilino-1,4-naphthoquinone (**1**) has been known since the first reports by Schultz, Zincke and Plimpton.[16] Since then, two general methods for the synthesis of derivatives of **1** have been developed: first, the oxidative coupling of alkyl and aryl amines with naphthoquinone;[17] and second, nucleophilic substitution reactions of 2-halonaphthoquinones[17c,18] or 2-methoxynaphthoquinone derivatives.[19] The first method is an example of a C(sp^2)-H bond transformation whereby a new C(sp^2)-N bond is formed at the expense of 2 electrons and 2 protons via an addition-oxidation reaction sequence.[20] It is therefore, in principle, an atom economical method for the construction of new bonds.[21] To this end, Lewis acids such as $CeCl_3$[22] have been used to promote the oxidative coupling reaction on the basis that they facilitate a Michael type addition to enone systems. However, a recent study has revealed how Ce(III) in the presence of oxygen results in the oxidation of 1,3-dicarbonyl systems and this maybe of relevance to the oxidative coupling of **2** and **3**.[23] The use of greater than stoichiometric quantities of Cu(II) salts in MeOH has been reported although long reaction times were required.[24] Specifically, a molar equivalent of hydrated copper acetate has been used for the oxidative coupling of alkylamines, present in large excess, with 1,4-naphthoquinone,[25] naphthazarin,[26] and juglone.[27] Additionally, nickel(II) salts were found to be beneficial in the oxidative addition reactions of amines with (iso)quinolindiones.[28]

Recent studies on the oxidative coupling of **2** and **3** to give **1** reported that the use of warm water was beneficial, resulting in excellent yields with only short reaction times.[29] Additionally, Tandon and Maurya reported the "on water" nucleophilic substitution and addition reactions with 1,4-quinones.[30] The use of a bentonitic clay was reported to give excellent yields (80−85%) for the oxidative coupling but required long reaction times. In the absence of the clay, yields were reduced to less than half.[31] Finally, the use of I_2 and ultrasonic irradiation was reported to give moderate to excellent yields of **1**,[32] while a gold(III) catalyzed reaction gave moderate to good yields of **1** via oxidative coupling of primary, or secondary, aliphatic and aromatic amines.[33]

RESULTS AND DISCUSSION

With the objective of studying concise routes into natural products, their analogues, and polyheteroaromatic systems with the 2-amino-1,4-(aza)naphthoquinone moiety, we initially investigated a synthetic protocol based upon earlier work by Thomson involving juglone derivatives and **2a** in ethanol.[17a,b] Heating **2a**

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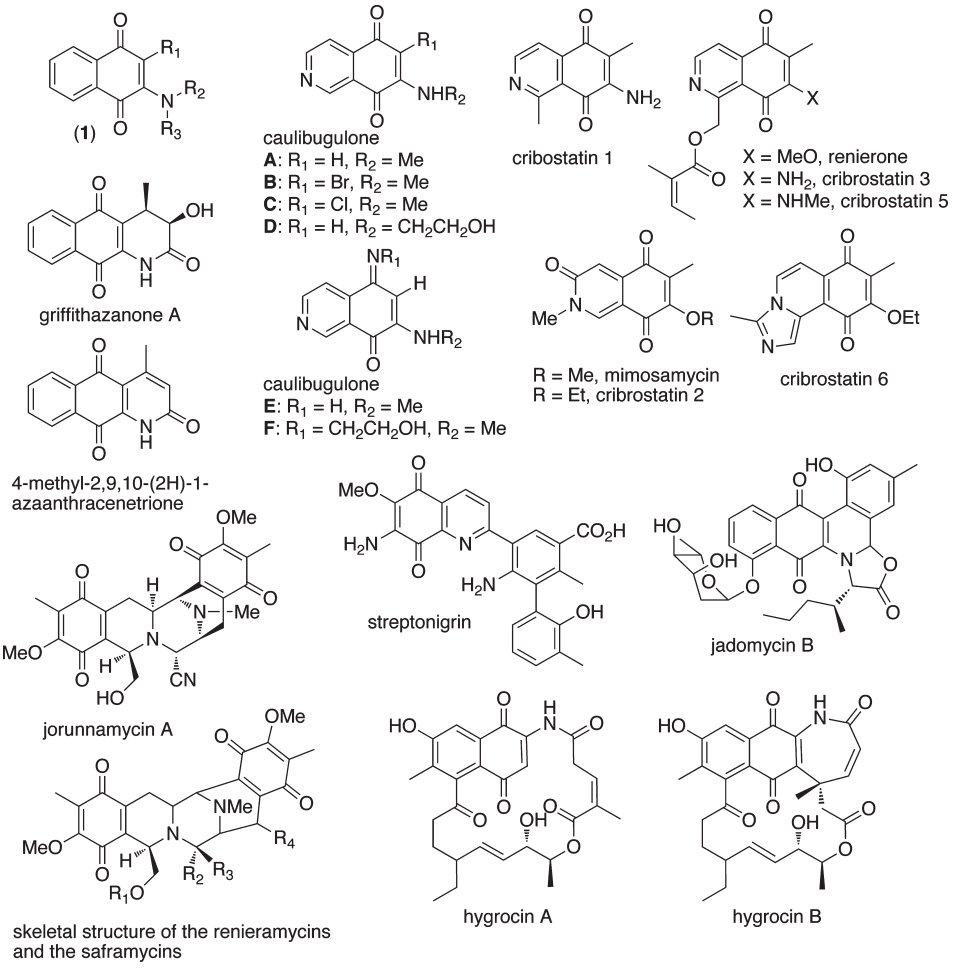

Figure 1. Some cytotoxic natural (aza)naphthoquinones.

and **3** in ethanol resulted in the precipitation of a dark-burgundy-colored solid. The solid was isolated by filtration and recrystallized from EtOAc to give **1a** in a modest yield of 35%. Analysis of the reaction by TLC revealed the extensive formation of colateral products. However, the yield could be improved by precipitating all materials from the ethanolic reaction by addition of water. The crude product obtained in this manner was purified by column chromatography, as summarized in Table 1/entry 1 (T1-E1), resulting in a moderate improvement of the purified yield of **1a**. Using a shorter heating period, a smaller yield was obtained (T1-E2). A subsequent reaction left for an additional period of time at room temperature gave a substantially better yield of **1a** (T1-E3). Changing the solvent from ethanol to AcOH and using a shorter heating period also gave a considerably better yield of **1a** (T1-E4 compared with E1). However, analysis of the AcOH reaction by TLC also revealed the presence of colateral products.

The currently considered mechanism for this coupling reaction (Scheme 1) initially involves a Michael addition of **2a** to **3** to give a dihydroquinone intermediate (**4**), which tautomerizes to the hydroquinone (**5**). Oxidation of **5** in the presence of molecular oxygen, or as a consequence of excess **3**, gives **1a**.

We suspected that the oxidation reaction could be responsible for the plethora of side products and therefore reasoned that the inclusion of an efficient, chemoselective, oxidizing agent would allow for a cleaner reaction with a better yield. A copper(II) salt, such as $Cu(OAc)_2.H_2O$ (**6**), seemed attractive as the Cu(I) reduction product is readily oxidized by atmospheric oxygen back to Cu(II). Indeed, when 10 mol % **6** was added to the reaction mixture (T1-E6 and E7), an extremely rapid reaction was observed to occur and **1a** crystallized from the reaction medium. TLC examination of the crude reaction revealed it to be surprisingly clean. The colateral products that had been observed in the previous oxidative coupling reactions were absent. The product **1a** was isolated by evaporation of the volatiles under reduced pressure, the solid was solubilized in CH_2Cl_2, and the solution was filtered through a short column of silica eluting with CH_2Cl_2 to remove the copper salts. After prolonged evaporation of the solvent under reduced pressure, **1a** was obtained in a very high yield of 97% (T1-E6 and E7). Notably, Inoue obtained a 53% yield of **1a** after bubbling air through a refluxing methanolic solution of **2a** and **3** during three hours in the presence of a molar equivalent of hydrated $Cu(OAc)_2$.[24a,b] The use of an acetonitrile/AcOH solution in the presence of **6**, followed by a similar workup, gave an 81% yield of **1a** (T1-E8) while the addition of the copper catalyst to an ethanolic reaction resulted in a 68% yield (T1-E5 compare with E2). A reduction of the quantity of the copper salt to 5 mol % gave an almost equally good yield after 50 min (compare T1-E9 with E7) while further reduction to about 2 mol % of copper salt gave a result similar to the absence of the catalyst (compare T1-E10 with E4). The use of water as a medium for agitating the reactants was briefly investigated (T1 entries

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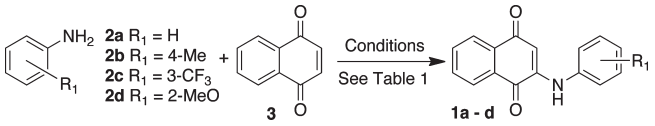
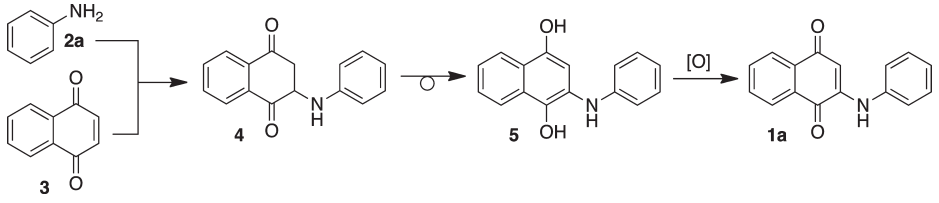
Table 1. Oxidative Coupling of 1,4-Naphthoquinone (3) with Amines (2) in the Absence and in the Presence of $Cu(OAc)_2.H_2O$ (6)



entry	amine[a] R-(NH_2)	$Cu(OAc)_2.H_2O$(mol %)	solvent[b]	time (mins)	yield (%)	mp (°C)[c]
1	Ph	0	EtOH (5)	120	55	188−9
2	Ph	0	EtOH	35	41	190−1
3	Ph	0	EtOH (5)	90 + 23 h rt	80	188−90
4	Ph	0	AcOH	80	76	191
5	Ph	10	EtOH	35	68	191−2
6	Ph	9	AcOH	30	97	190
7	Ph	10	AcOH	25	97	190
8	Ph	11	AcOH (1):ACN (4)	40	81	188−90
9	Ph	5	AcOH	50	93	189−90
10	Ph	2	AcOH	65	71	191−2
11	Ph	0	H_2O (25)[d]	60	16	184−6
12	Ph	14	H_2O (25)[d]	60	63	185−6
13[e]	Ph	10	AcOH (20)	60	66	191−2
14[e,f]	Ph	10	AcOH (20)	60	78	191−2
15	4-MePh	0	EtOH (3)	120	35	199−200
16	4-MePh	9	AcOH	20	82	197−200
17	3-CF_3Ph	0	AcOH	60	63	171−3
18	3-CF_3Ph	13	AcOH	30	90	173−4
19	2-MeOPh	0	AcOH	60	75	147−8
20	2-MeOPh	12	AcOH	40	97	147−8

[a] R-NH_2: R = Ph, aniline; R = 4-MePh, *p*-toluidine; R = 3-CF_3Ph, 3-trifluoromethylaniline; R = 2-MeOPh, 2-methoxyaniline. [b] 1,4-Naphthoquinone (1 mmol) and amine (1 mmol), with or without $Cu(OAc)_2.H_2O$, were heated (65 °C) in 2 mL of solvent unless otherwise indicated by a value in parentheses. [c] R = Ph: mp (lit.): 189−190 °C;[31] R = 4-MePh: mp (lit.): 200−201 °C;[32] and R = 3-CF_3Ph mp (lit.): 174 °C;[24c] and R = 2-MeOPh: mp (lit.): 146 °C.[34] [d] A larger volume of water was used in relation to the other solvents due to the poor solubility of **3**, but even under the conditions used **3** was incompletely soluble. [e] A 10-fold increase in the scale of the reaction. The reactions are exothermic on addition of the aniline and the internal temperature rose from 60 °C to about 75 °C. The crude products obtained, after evaporation of the volatiles, were solubilized in CH_2Cl_2 and filtered through a short column of silica gel eluting with CH_2Cl_2 (respective mass balances for table entries 13 and 14 were 82% and 93%). The products were then recrystallized from EtOH/H_2O (aprox. 2:1 V/V). The yields given in the table are for the first crop of crystals. A further crop of crystals can be obtained by concentration of the filtrates, filtration, and recrystallization of the solids from a respectively smaller volume of EtOH/H_2O. [f] An atmosphere of oxygen was used.

Scheme 1. Schematic Representation of the Mechanism for Oxidative Coupling of Aniline and 1,4-Naphthoquinone



11 and 12) and reactions were intentionally terminated after 60 min. Despite the inferior results, the use of the copper salt as an additive was revealed to be a significant advantage. Further, the reaction of **2a** with **3** was conducted on a 10-fold larger scale. In the first instance (T1-E13), the reaction was stirred open to the atmosphere where it was noted that copper was deposited onto the surface of the reaction vessel, and that the reaction mixture did not crystallize, during the reaction. Repetition of the 10-fold larger scale reaction but using an atmosphere of oxygen (T1-E14) resulted in the crystallization of the reaction product within the first 30 min (as in T1-E6 and E7), and no evidence for the deposition of copper metal was observed during the reaction. The experiments clearly indicate how the mass transfer of oxygen during the reaction influences the outcome of the reaction.

In a similar manner, the aniline derivatives **2b**−**d** were subjected to oxidative coupling with **3** in the presence and absence of

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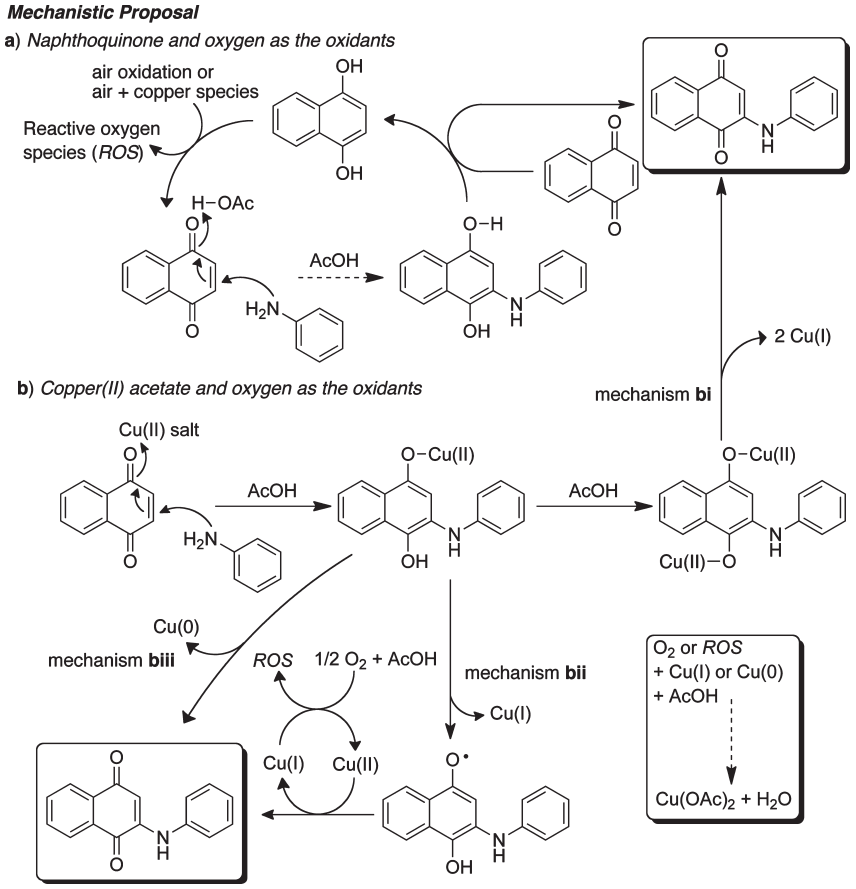
Scheme 2. Schematic Representation of the Proposed Participation of Cu(II) in the Oxidative Coupling of Anilines and 1,4-Naphthoquinone



10 mol % **6**. The results reveal in all cases that the reactions incorporating the copper salt, and using AcOH as the solvent, give superior yields in shorter reaction times (T1-E15 to E20).

The results from the experiments as summarized in Table 1 reveal the value of adding a catalytic quantity of **6** to the reaction. Scheme 2 depicts a proposal for the reaction mechanism with the participation of Cu^{2+}.

In support of the proposed mechanism, copper(II) ions are known to oxidize hydroquinones to the respective quinones. Whereas in the present study the end oxidant is atmospheric oxygen, catalytic studies of the oxidation of hydroquinone have generally used hydrogen peroxide as the stoichiometric oxidant.[35] In Scheme 2, Michael addition of **2** to **3** could be facilitated by either protonation of **3** or complexation of **6** to **3**. The resulting copper hydroquinone complex could interact directly with oxygen to give the quinone product or could pass through sequential one electron oxidation steps where the resulting Cu(I) species would then be reoxidized to Cu(II) by oxygen. The oxygen should eventually be reduced to water and this may occur through the formation of reactive oxygen species (ROS). In the absence of the copper salt, the ROS maybe responsible for the formation of colateral products. Therefore, the presence of the copper salt may also serve to eliminate the ROS.

ESI-MS monitoring of reactions has proven to be a versatile method for the interception and characterization of actual reaction intermediates.[36] To this end, extensive experimentation was conducted but the only copper species reliably observed was the copper cation as the isotopologues $^{63}Cu(I)(ACN)_2^+$ (m/z 145) and $^{65}Cu(I)(ACN)_2^+$ (m/z 147) in an approximately 2:1 ratio. The observation of this ion is consistent with the facile reduction of the initial Cu(II) salt under the reaction conditions. The difficulty in detecting copper ion reaction intermediates by ESI-MS in this case, is probably related to their very transient nature and the facility with which they undergo decomposition.[37] It is notable that Cu(I) phenoxide species are oxygen (air) sensitive compounds that have only been adequately characterized by the inclusion of ligands or ligating groups in the Cu(I) coordination sphere.[38]

A thorough literature search turned up a few more examples of oxidative addition reactions of quinones, other than **3**, that envolved the participation of copper salts. Matsuoka and colleagues observed that a large excess of butylamine reacts with 5,8-dihydroxy-1,4-naphthoquinone in the presence of 2 mol equivalents of copper(II) salts to give a variety of products resulting from both nucleophilic substitution of the hydroxyl groups and oxidative coupling,[39] whereas the analogous reaction with 1,4-dihydroxyanthraquinone selectively gave 2-butylamino-1,4-dihydroxyanthraquinone.[40] A similar reaction with ethylenediamine gave a product resulting from oxidative addition and cyclization.[41] Yoshida and co-workers found that *N*-alkylanilines regioselectively react at the 6-position with quinolin-5,8-dione in the presence of a molar equivalent of copper(II) acetate to give mixtures of products resulting from oxidative coupling to both the para position and the nitrogen of the aniline derivative.[28c] Kitahara

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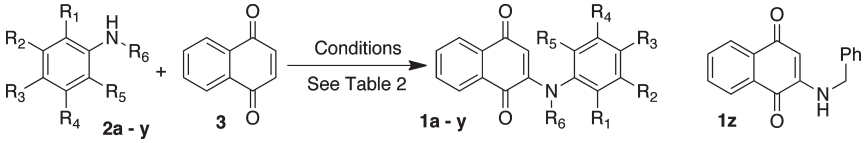
Table 2. Oxidative Coupling of Amines (2a−z) with 1,4-Naphthoquinone (3) in the Presence of 10 mol % $Cu(OAc)_2.H_2O$ in AcOH (approx. 60 °C) in Air



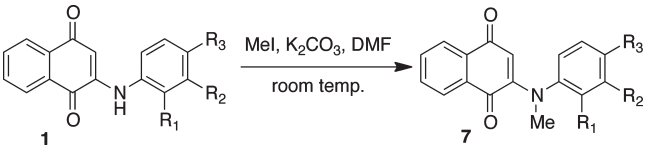
	R1−6[a]	time (mins)[b]	yield (%)		R1−6[a]	time (mins)[b]	yield (%)
a	R1−6 = H	25	97	**n**	R2 = NO_2	40	82
b	R3 = Me	20	82	**o**	R3 = F	30	73
c	R2 = CF_3	30	90	**p**	R3 = Cl	30	87
d	R1 = OMe	40	97	**q**	R3 = Br	30	85
e	R3 = OMe	30	92	**r**	R1 = I	30	71
f	R2 = OMe	30	93	**s**	R2 = Cl, R3 = OMe	40	63
g	R3 = CN	240	32	**t**	R1 = OMe, R4= Cl	40	99
h	R2 = CN	240	40	**u**	R1 = OMe, R3 = NO_2	240	88
i	R1 = CN	240	78	**v**	R1 = Me, R3 = MeO	30	90
j	R3 = CO_2H	40	68	**w**	R1, R5 = Me	180	55
k	R2 = CO_2H	25	64	**x**	R1, R4 = OMe	25	42
l	R1 = CO_2H	40	63	**y**	R6 = Me	70	74
m	R3 = NH2	65	24	**z**	Bn(c)[c]	80	50

[a] R_{1-6} = H unless otherwise indicated. [b] The reactions were followed by TLC until the apparent consumption of the limiting substrate. [c] Benzylamine was used.

and co-workers as part of their synthetic studies on the preparation of isoquinolindiones reported the oxidative coupling of amines with 5-isoquinolinol to give 8-dialkylamino-5,6-isoquinolinediones and the 7-isoquinolinol to give 3,5-(dialkylamino)-7,8-isoquinolinediones in the presence of 50 mol % copper(II) acetate.[42] However, more recently Park and co-workers reported the use of copper nanoparticles entrapped in aluminum oxyhydroxide for the oxidative coupling of amines with hydroquinones in ethyl acetate.[35e] In building upon these precedents, the present study has found that catalytic quantities (10 mol %) of **6** in AcOH result in good to excellent yields for the regiospecific oxidative coupling of anilines with **3** in very short reaction times.

The copper acetate/AcOH methodology was subsequently applied to a variety of substituted anilines and benzylamine. The results are detailed in Table 2. A few observations but no general trends can be made with respect to the results: the cyano-anilines (**2g**, **2h** and **2i**), and aniline **2u**, all required a longer period of heating but only **2i** and **2u** gave good yields of the respective products **1i** and **1u**; the carboxylic acids (**1j**, **1k** and **1l**) were isolated by precipitating with water and washed with ethanol, this procedure may account for the lower yields; the product **1m** from aniline **2m** was difficult to purify from the reaction mixture; the hindered 2,6-dimethylaniline (**2w**) gave a reduced yield and required a longer period of heating in comparison to other aniline derivatives that did not have two *ortho* substituents; aniline **2x** gave a lower yield in comparison to the other disubstituted methoxyaniline derivatives possibly due to it being easily oxidized; and *N*-methyl aniline **2y** required a slightly longer reaction time, and gave a reduced yield of **1y** in comparison to the formation of **1a**. The products were physically and spectroscopically characterized. In a number of cases, the derivatives of **1** were poorly soluble in commonly used NMR solvents. Therefore,

Scheme 3. *N*-Methylation of Derivatives of 1 to Give 7[a]



[a] R_1, R_2 and R_3 = H unless otherwise stated. **7g** R_3 = CN, 80%; **7k** R_2 = CO_2Me, 87%; **7o** R_3 = F, 90%; **7p** R_3 = Cl, 58%; **7q** R_3 = Br, 60%; **7s** R_2 = Cl, R_3 = MeO, 73%; **7u** R_1 = MeO, R_3 = NO_2, 68%.

some of the derivatives **1** were *N*-methylated by reaction with MeI in the presence of K_2CO_3 in DMF to give **7** (Scheme 3) with the intention of improving their solubility for analysis by ^1H and ^{13}C NMR. Kallmayer has reported an alternative methodology for the *N*-alkylation of **1**.[43]

CONCLUSION

The inclusion of a catalytic quantity of $Cu(OAc)_2.H_2O$ in the oxidative coupling of anilines (**2**) with naphthoquinone (**3**), resulting in the $C(sp^2)$-H functionalization of **3**, was found to have a beneficial effect upon both the time required for reaction to complete and in eliminating or reducing the formation of side products. No systematic effect of the substituents on **2** was observed, although steric hindrance due to two *ortho*-substituents may reduce the yield.

EXPERIMENTAL SECTION

General. The solvents and reagents used in the present study were purchased from commercial suppliers and were used as received. Thin layer chromatography was performed with fluorescent silica coated

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aluminum sheets. Silica gel (70−230 mesh) was used for column chromatography.

Reaction products were characterized by nuclear magnetic resonance spectroscopy (^{1}H - 200 MHz, ^{13}C - 50 MHz). The ^{1}H NMR spectra data is expressed in the form: Chemical shift in units of ppm (normalized integration, multiplicity, the value of *J* in Hz). The multiplicity of the observed signals is expressed as: s (singlet), d (doublet), t (triplet), m (multiplet) or a combination thereof, for example dd (doublet of doublets). The Fourier transform infrared spectra were obtained as KBr pellets. High resolution mass spectra (HRMS) were obtained by dissolving compounds (1 mg) in methanol (1 mL, HPLC grade). For an analysis in the positive ion mode, a total of 2 μL of a 1% aqueous solution of formic acid was added into the same volume. Direct infusion automated chip-based nano-ESI-MS was performed. Samples were loaded into 96-well plates (total volume of 100 μL in each well) and analyzed using a Fourier transform mass spectrometer. ESI general conditions were: gas pressure of 0.3 psi and capillary voltage of 1.55 kV. Mass spectra were the result of over 100 microscans, centered, and aligned using the supplied software. Melting points were recorded in open capillaries and are uncorrected.

General Experimental Procedure. 1,4-Naphthoquinone hydrate (**3**) (1 mmol) and hydrated $Cu(OAc)_2$ (0.1 mmol) were solubilized by gently warming in AcOH (2 mL). Amine (**2**) (1 mmol) was added and the reaction was gently warmed (60−70 °C). After the indicated reaction time, all the volatiles were removed under reduced pressure irrespective of complete or incomplete consumption of the reagents. The resulting crude product was taken up in a minimal volume of CH_2Cl_2 and applied to a column of silica gel. The column was eluted with CH_2Cl_2 and the product, generally a dark burgundy colored or a dark red colored band, was readily separated from any impurities. Where other solvents or mixtures were used, these are indicated with the description of each product. The solvent was removed under reduced pressure to give 2-amino-1,4-naphthoquinone derivatives (**1a**−**z**).

Physical and Spectroscopic Characterization Data for Compounds 1a−z. ***1a*** *2-(Phenyl)amino-1,4-naphthoquinone.* M.p.: 191−2 °C; (lit.): 189−190 °C.[31] IR (cm^{-1}): 3318, 1668, 1639, 1609, 1596, 1572, 1528, 1354, 1304, 776, 752, 724, 709. HRMS (*m*/*z*): Obs. 250.0863; Calcd 250.0868 ($C_{16}H_{12}NO_2^+$). ^{1}H NMR (pyridine-d_5 + DMSO-d_6): 6.40 (1H, s); 7.30 (1H, m); 7.52 (4H, m); 7.76 (1H, m); 7.86 (1H, m); 8.17 (2H, m); 9.59 (1H, s). ^{13}C NMR: 102.6; 124.1; 125.7; 125.8; 126.5; 129.7; 131.0; 132.8; 133.3; 135.0; 138.7; 146.7; 182.1; 183.3.

1b *2-(4-Methylphenyl)amino-1,4-naphthoquinone.* M.p.: 199−200 °C; (lit.): 200−201 °C.[32] IR (cm^{-1}): 3325; 1668; 1636; 1603; 1571; 1526; 1349; 1304; 1290; 774; 724. HRMS (*m*/*z*): Obs. 264.1019; Calcd 264.1025 ($C_{17}H_{14}NO_2^+$). ^{1}H NMR (pyridine-d_5/DMSO-d_6): 2.26 (3H, s); 6.52 (1H, s); 7.20 (2H, d, 8.0); 7.37 (2H, d, 8.0); 7.65 (2H, m); 8.17 (2H, d, 8.0); 8.31 (2H, d, 8.0); 9.80 (1H, s). ^{13}C NMR: 20.4; 101.7; 123.7; 125.3; 126.0; 129.7; 130.5; 132.3; 132.7; 134.6; 134.7; 135.5; 146.4; 181.7; 182.5.

1c *2-(3-Trifluoromethylphenyl)amino-1,4-naphthoquinone.* M.p.: 173−4 °C; (lit.): 174 °C.[24c] IR (cm^{-1}): 3235; 1677; 1623; 1574; 1528; 1334; 1245; 1121; 1074; 994; 779; 722; 698. HRMS (*m*/*z*): Obs. 318.0737; Calcd 318.0742 ($C_{17}H_{11}F_3NO_2^+$). ^{1}H NMR (DMSO-d_6): 6.15 (1H, s); 7.52 (1H, d, 8.0); 7.82 (6H, m); 8.04 (1H, dd, 2.0, 8.0); 9.39 (1H, s). ^{13}C NMR: 103.1; 119.9; 121.2; 125.3; 126.1; 126.9; 130.4; 130.5; 132.4; 132.8; 134.2; 134.9; 138.7; 139.2; 145.7; 181.3; 182.8.

1d *2-(2-Methoxyphenyl)amino-1,4-naphthoquinone.* M.p.: 147−8 °C; (lit.): 146 °C.[34] IR (cm^{-1}): 3307; 1672; 1617; 1575; 1533; 1487; 1463; 1292; 1248; 1190; 1110; 1028; 988; 752; 727; 542. HRMS (*m*/*z*): Obs. 280.0964; Calcd 280.0974 ($C_{17}H_{14}NO_3^+$). ^{1}H NMR (pyridine-d_5+DMSO-d_6): 3.76 (3H, s); 6.02 (1H, s); 7.00 (1H, t, 8.0); 7.06 (1H, d, 8.0); 7.20 (1H, t, 8.0); 7.39 (1H, d, 8.0); 7.67 (1H, t, 8.0); 7.77 (1H, t, 8.0); 8.03 (2H, d, 8.0); 8.77 (1H, s). ^{13}C NMR: 55.6; 102.8; 112.0; 120.8; 123.6; 125.5; 126.1; 126.4; 126.6; 130.4; 132.4; 132.9; 134.8; 145.3; 152.2; 181.6; 182.7.

1e *2-(4-Methoxyphenyl)amino-1,4-naphthoquinone.* M.p.: 154−5 °C; (lit.): 155−6 °C.[29] IR (cm^{-1}): 3222; 1678; 1615; 1597; 1566; 1507; 1357; 1292; 1234; 1173; 1123; 1041; 991; 830; 778; 722. HRMS (*m*/*z*): Obs. 280.0963; Calcd 280.0974 ($C_{17}H_{14}NO_3^+$). ^{1}H NMR (DMSO-d_6): 3.77 (3H, s); 5.92 (1H, s); 7.00 (2H, d, 8.0); 7.29 (2H, d, 8.0); 7.9 (4H, m); 9.15 (1H, s). ^{13}C NMR: 55.3; 101.0; 114.5; 125.2; 125.6; 126.0; 130.6; 132.4; 134.8; 138.7; 146.9; 156.9; 181.6; 182.2.

1f *2-(3-Methoxyphenyl)amino-1,4-naphthoquinone.* The products from the two reactions were purified by silica gel column chromatography eluting with CH_2Cl_2. Bright red crystals. M.p.: 160−163 °C; (lit.): 172 °C.[34] IR (cm^{-1}): 3327; 1676; 1606; 1594; 1568; 1530; 1500; 1351; 1298; 1265; 1242; 1215; 1160; 1120; 1002; 869; 775; 726. HRMS (*m*/*z*): Obs. 280.0968; Calcd 280.0974 ($C_{17}H_{14}NO_3^+$). ^{1}H NMR (DMSO-d_6): 3.77 (3H, s); 6.15 (1H, s); 6.79 (1H, d, 8.0); 6.95 (1H, s); 6.97 (1H, d, 8.0); 7.34 (1H, t, 8.0); 7.76 (1H, td, 2.0, 8.0); 7.85 (1H, td, 2.0, 8.0); 7.95 (1H dd, 2.0, 8.0); 8.04 (1H, dd, 2.0, 8.0); 9.17 (1H, s). ^{13}C NMR: 55.2; 102.5; 109.4; 110.7; 115.5; 125.3; 126.1; 130.0; 130.4; 132.5; 132.6; 134.9; 139.3; 146.0; 159.9; 181.5; 182.6.

1g *2-(4-Cyanophenyl)amino-1,4-naphthoquinone.* The products from the two reactions were purified by silica gel column chromatography eluting with CH_2Cl_2. Red crystals. M.p.: Exp. 1. 302−306 °C; Exp. 2. 302−304 °C. IR (cm^{-1}): 3204; 2222; 1676; 1638; 1598; 1571; 1530; 1502; 1415; 1356; 1298; 992; 835; 776; 724. HRMS (*m*/*z*): Obs. 275.0819; Calcd 275.0821 ($C_{17}H_{11}N_2O_2^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1h *2-(3-Cyanophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with EtOAc. Red crystals. M.p.: 290−291 °C; (lit.): 296−298 °C.[22b] IR (cm^{-1}): 3183; 2227; 1677; 1622; 1574; 1524; 1357; 1301; 1125; 776; 723; 679. HRMS (*m*/*z*): Obs. 275.0811; Calcd 275.0821 ($C_{17}H_{11}N_2O_2^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1i *2-(2-Cyanophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Orange crystals. M.p.: 225−227 °C. IR (cm^{-1}): 3326; 2222; 1674; 1645; 1620; 1576; 1530; 1453; 1346; 1295; 1271; 991; 757; 718. HRMS (*m*/*z*): Obs. 275.0817; Calcd 275.0821 ($C_{17}H_{11}N_2O_2^+$). ^{1}H NMR (DMSO-d_6): 5.70 (1H, s); 7.50 (1H, t, 8.0); 7.60 (1H, d, 8.0); 7.82 (3H, m); 7.96 (2H, m); 8.08 (1H, dd, 2.0, 8.0); 9.43 (1H, s). ^{13}C NMR: 103.6; 109.4; 116.5; 125.4; 126.2; 127.0; 127.1; 130.2; 132.3; 132.9; 133.9; 134.5; 135.0; 140.6; 146.7; 181.0; 182.6.

1j *4-(2-Amino-1,4-naphthoquinone) benzoic acid.* The crude products from the three experiments were suspended in EtOH and filtered. The residues, red crystals, were washed with EtOH. M.p.: Exp. 1. 319−321 °C; Exp. 2. 317−320 °C; (lit.): 319 °C.[44] IR (cm^{-1}): 3469; 3369; 3187; 3077; 1682; 1639; 1599; 1573; 1526; 1421; 1307; 1292; 1274; 1249; 1183; 992; 845; 776; 721. HRMS (*m*/*z*): Obs. 294.0763; Calcd 294.07663 ($C_{17}H_{12}NO_4^+$)

The product has very poor solubility in solvents commonly used for NMR analysis.

1k *3-(2-Amino-1,4-naphthoquinone) benzoic acid.* The crude product was suspended in EtOH and filtered. The residue, orange crystals, was washed with EtOH. M.p.: 264−265 °C; (lit.): 254 °C.[44] IR (cm^{-1}): 3551; 3479; 3414; 3295; 3222; 3069; 1699; 1679; 1605; 1574; 1533; 1418; 1355; 1299; 775; 754; 720; 679. HRMS (*m*/*z*): Obs. 294.0756; Calcd 294.0766 ($C_{17}H_{12}NO_4^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1l *2-(2-Amino-1,4-naphthoquinone) benzoic acid.* The crude product was suspended in EtOH and filtered. The residue, red crystals, was washed with EtOH. M.p.: 237−40 °C decomp. with gas evolution; (lit.):

265 °C.[44] IR (cm^{-1}): 3456; 3276; 1686; 1608; 1567; 1534; 1358; 1296; 1210; 1152; 1083; 777; 752; 721. HRMS (m/z): Obs. 294.0757; Calcd 294.0766 ($C_{17}H_{12}NO_4^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1m *2-(4-Aminophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with EtOAc. Burgundy crystals. M.p.: 205−210 °C; (lit.): 214 °C.[45] IR (cm^{-1}): 3415; 3315; 1671; 1630; 1600; 1570; 1513; 1354; 1297; 1268; 1248; 992; 817; 773; 725; 496. HRMS (m/z): Obs. 265.0967; Calcd 265.0977 ($C_{16}H_{13}N_2O_2^+$). ^{1}H NMR (pyridine-d_5 + DMSO-d_6): 6.22 (1H, s); 6.97 (2H, d, 8.0); 7.27 (2H, d, 8.0); 7.90 (4H, m); 9.41 (1H, s); 4-NH_2 group not observed due to the presence of water in the deuterated solvents. ^{13}C NMR: 100.7; 114.4; 125.3; 125.4; 125.9; 126.3; 130.6; 131.9; 133.2; 134.5; 147.2; 147.2; 182.0; 182.1.

1n *2-(3-Nitrophenyl)amino-1,4-naphthoquinone.* Recrystallized from EtOAc after hot filtration. Orange crystals. M.p.: 258−262 °C; (lit.): 252−255 °C;[19c] 258−260 °C.[22b] IR (cm^{-1}): 3293; 3219; 1676; 1626; 1606; 1576; 1527; 1354; 1300; 1273; 719. HRMS (m/z): Obs. 295.0718; Calcd 295.0719 ($C_{16}H_{11}N_2O_4^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1o *2-(4-Fluorophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Bright red crystals. M.p.: 246−248 °C; (lit.): 227 °C;[24c] 248−9 °C.[46] IR (cm^{-1}): 3319; 1667; 1640; 1611; 1574; 1508; 1352; 1301; 1231; 827; 776; 725. HRMS (m/z): Obs. 268.0770; Calcd 268.0774 ($C_{16}H_{11}FNO_2^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1p *2-(4-Chlorophenyl)amino-1,4-naphthoquinone.* A mixture of 30% EtOAc in hexane was added to the reaction mixture and the suspension was filtered then washed with the same solvent mixture. Bright red crystals. M.p.: 250−253 °C; (lit.): 248−249 °C;[31] 264 °C.[24a] IR (cm^{-1}): 3201; 1679; 1621; 1607; 1571; 1519; 1492; 1357; 1300; 1288; 825; 775; 723. HRMS (m/z): Obs. 284.0476; Calcd 284.0478 ($C_{16}H_{11}ClNO_2^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1q *2-(4-Bromophenyl)amino-1,4-naphthoquinone.* The product was purified by silica gel column chromatography eluting with CH_2Cl_2 followed by a CH_2Cl_2/EtOAc gradient with up to 20% EtOAc. Bright red crystals. M.p.: 258−262 °C (recryst. EtOAc). IR (cm^{-1}): 3209; 1679; 1634; 1605; 1568; 1514; 1488; 1402; 1358; 1299; 1287; 823; 777; 723. HRMS (m/z): Obs. 327.9972; Calcd 327.9973 ($C_{16}H_{11}BrNO_2^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1r *2-(2-Iodophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Orange crystals. M.p.: 156−158 °C. IR (cm^{-1}): 3301; 1680; 1614; 1603; 1564; 1487; 1478; 1469; 1349; 1331; 1307; 1253; 1119; 1018; 989; 842; 780; 727; 721; 553. HRMS (m/z): Obs. 375.9823; Calcd 375.9835 ($C_{16}H_{11}INO_2^+$). ^{1}H NMR (pyridine-d_5 + DMSO-d_6): 5.69 (1H, s); 7.05 (1H, m); 7.44 (1H, m); 7.73 (3H, m); 8.03 (3H, m); 9.32 (1H, s). ^{13}C NMR: 97.7; 102.9; 125.5; 126.0; 127.1; 128.5; 129.5; 130.4; 132.4; 132.8; 134.7; 139.7; 139.7; 146.7; 181.3; 182.6.

1s *2-(3-Chloro-4-methoxyphenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2 followed by a CH_2Cl_2/EtOAc gradient up to 20% EtOAc. Burgundy crystals. M.p.: 235−237 °C. IR (cm^{-1}): 3212; 1678; 1630; 1618; 1596; 1577; 1500; 1359; 1259; 1120; 1063; 1026; 996; 779; 722. HRMS (m/z): Obs. 314.0582; Calcd 314.0584 ($C_{17}H_{13}ClNO_3^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1t *2-(2-Methoxy-5-chlorophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2 followed by a CH_2Cl_2/EtOAc gradient up to 20% EtOAc. Burgundy crystals. M.p.: 160−163 °C. IR (cm^{-1}): 3201; 1680; 1622; 1606; 1570; 1520; 1493; 1406; 1358; 1300; 1288; 1238; 1124; 1095; 824; 825; 775; 723. HRMS (m/z): Obs. 314.0573; Calcd 314.0584 ($C_{17}H_{13}ClNO_3^+$). ^{1}H NMR (DMSO-d_6): 3.84 (3H, s); 5.72 (1H, s); 7.17 (1H, d, 8.0); 7.32 (1H, dd, 8.0, 2.0); 7.37 (1H, d, 2.0); 7.78 (1H, t, 8.0); 7.84 (1H, d, 8.0); 7.93(1H, t, 8.0); 8.04 (1H, d, 8.0); 8.69 (1H, s). ^{13}C NMR: 56.1; 103.6; 113.7; 123.9; 124.2; 125.4; 126.1; 126.4; 127.5; 130.2; 132.5; 132.8; 135.0; 145.2; 151.4; 181.3; 182.5.

1u *2-(2-Methoxy-4-nitrophenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Orange crystals. M.p.: 236−238 °C. IR (cm^{-1}): 3276; 1673; 1638; 1626; 1589; 1578; 1546; 1518; 1489; 1339; 1291; 1272; 1247; 1095; 1024; 741. HRMS (m/z): Obs. 325.0824; Calcd 325.0825 ($C_{17}H_{13}N_2O_5^+$).

The product has very poor solubility in solvents commonly used for NMR analysis.

1v *2-(2-Methyl-4-methoxyphenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Bright red crystals. M.p.: 121−124 °C. IR (cm^{-1}): 3361; 2943; 1672; 1638; 1575; 1530; 1493; 1349; 1331; 1304; 1256; 1116; 1022; 829; 810; 775; 719; 666; 592. HRMS (m/z): Obs. 294.1120; Calcd 294.1130 ($C_{18}H_{16}NO_3^+$). ^{1}H NMR (pyridine-d_5 + DMSO-d_6): 2.20 (3H, s); 3.74 (3H, s); 6.08 (1H, s); 6.98 (2H, m); 7.20 (1H, s); 7.68 (1H, t, 7.0); 7.78 (1H, t, 7.0); 8.06 (2H, d, 7.0); 8.79 (1H, s, NH). ^{13}C NMR: 20.0; 55.5; 102.7; 111.7; 124.0; 125.3; 125.97; 126.03; 126.8; 129.8; 130.3; 132.3; 132.8; 134.6; 145.2; 150.0; 181.6; 182.5.

1w *2-(2,6-Dimethylphenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Orange crystals. M.p.: 186−190 °C. IR (cm^{-1}): 3288; 1678; 1625; 1605; 1590; 1572; 1492; 1352; 1300; 1247; 1121; 987; 842; 777; 727; 523. HRMS (m/z): Obs. 278.1176; Calcd 278.1181 ($C_{18}H_{16}NO_2^+$). ^{1}H NMR (DMSO-d_6): 2.14 (6H, s); 4.93 (1H, s); 7.20 (3H, s); 7.80 (3H, m); 8.06 (1H, d, 8.0); 9.06 (1H, s, NH). ^{13}C NMR: 17.5; 100.6; 125.3; 126.0; 127.6; 128.4; 130.6; 132.4; 133.0; 134.6; 134.8; 135.5; 147.7; 181.3; 181.9.

1x *2-(2,5-Dimethoxyphenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Burgundy crystals. M.p.: 99−101 °C. IR (cm^{-1}): 3350; 2945; 1674; 1638; 1601; 1575; 1534; 1493; 1348; 1331; 1306; 1250; 1217; 1116; 1047; 1022; 777; 721. HRMS (m/z): Obs. 310.1069; Calcd 310.1079 ($C_{18}H_{16}NO_4^+$). ^{1}H NMR (pyridine-d_5 + DMSO-d_6): 3.70 (3H, s); 3.73 (3H, s); 6.07 (1H, s); 6.81 (1H, dd, 2.0, 8.0); 7.02 (1H, d, 8.0); 7.03 (1H, d, 2.0); 7.68 (1H, t, 8.0); 7.78 (1H, t, 8.0); 8.05 (2H, d, 8.0); 8.80 (1H, s). ^{13}C NMR: 55.4; 55.9; 103.2; 110.0; 110.7; 112.8; 125.4; 126.0; 127.1; 130.4; 132.4; 132.8; 134.7; 145.1; 146.4; 153.4; 181.5; 182.6.

1y *N-Methyl-2-(phenyl)amino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Bright red crystals. M.p.: 189−191 °C; (lit.): 186−188 °C.[47] IR (cm^{-1}): 3064; 2924; 1674; 1626; 1589; 1560; 1492; 1371; 1346; 1288; 1263; 1135; 949; 782; 769; 727; 698. HRMS (m/z): Obs. 264.1014; Calcd 264.1025 ($C_{17}H_{14}NO_2^+$). ^{1}H NMR ($CDCl_3$): 3.31 (3H, s); 6.03 (1H, s); 7.02 (1H, d, 8); 7.03 (1H, d, 8); 7.17 (1H, t, 8); 7.30 (2H, m); 7.50 (1H, td, 2, 8); 7.60 (1H, td, 2, 8); 7.79 (1H, dd, 2, 8); 7.97 (1H, dd, 2, 8). ^{1}H NMR (DMSO-d_6): δ 7.94 (1H, m), 7.77 (3H, m), 7.36 (2H, m), 7.21 (3H, m), 6.15 (1H, s), 3.34 (N-Me+water from solvent). ^{13}C NMR (DMSO-d_6): 42.9; 111.7; 124.9; 125.0; 125.5; 126.2; 129.2; 132.0; 132.1; 132.8; 134.1; 148.0; 151.9; 181.6; 182.4.

1z *2-N-Benzylamino-1,4-naphthoquinone.* Purified by silica gel column chromatography eluting with CH_2Cl_2. Red crystals. M.p.: 155 °C; (lit.): 158−9 °C;[32] 160−1 °C.[48] IR (cm^{-1}): 3333; 1681; 1606; 1595; 1562; 1504; 1362; 1338; 1259; 1124; 729. ^{1}H NMR (DMSO-d_6): 4.44 (2H, d, 6.0); 5.53 (1H, s); 7.32 (5H, s); 7.85 (4H, m); 8.13 (1H, bs). ^{13}C NMR: 45.4; 100.6; 125.5; 126.1; 127.3; 127.4; 128.7; 130.5; 132.5; 133.2; 135.1; 137.5; 148.7; 181.7; 181.8.

*N-Methylation of 2-(R-Phenyl)amino-1,4-naphthoquinone Derivatives (**1**).* Because of the poor solubility of a number of the derivatives **1**, some of these compounds were *N*-methylated with the intention of improving their solubility so as to be able to characterize the *N*-methylated derivative by ^{1}H and ^{13}C NMR.

General Experimental Protocol. To a round bottomed flask were added: K_2CO_3 (3 mmol), the 2-phenylamino-1,4-naphthoquinone derivative **1** (1 mmol), methyl iodide (1−2 mL), and DMF (1−2 mL). The reaction flask was closed with a septum but allowed to pressure equalize with the atmosphere via an open syringe needle. The reaction mixture was stirred at room temperature and periodically monitored by TLC. After the indicated reaction time (not optimized), all volatiles were removed under reduced pressure to give a crude product that was taken up in CH_2Cl_2 and applied to a column of silica gel. Eluting the column with CH_2Cl_2 readily separated the *N*-methylated products **7**.

Physical and Spectroscopic Characterization of 7. ***7g*** *N-Methyl-2-(4-cyanophenyl)amino-1,4-naphthoquinone.* Reaction time 114 h, Red crystals, 80% yield. M.p.: 173−6 °C; IR (cm^{-1}): 3091; 3055; 2225; 1674; 1630; 1591; 1381; 1327; 1296; 1267; 1138; 789; 723; 577. ^{1}H NMR ($CDCl_3$): 8.07 (1H, dd, 8, 2), 7.89 (1H, dd, 8, 2), 7.73 (2H, m), 7.63 (2H, d, 8), 7.14 (2H, d, 8), 6.36 (1H, s), 3.39 (3H, s). ^{13}C NMR ($CDCl_3$): 183.9; 181.5; 151.9; 151.3; 134.4; 133.5; 133.2; 132.4; 132.2; 127.0; 126.0; 124.7; 118.6; 116.5; 108.6; 42.4.

7k *Methyl N-Methyl-(2-N-1,4-naphthoquinone)-3-amino-benzoate.* Reaction time 20 h, Bright red crystals, 87% yield. M.p.: 148−150 °C; IR (cm^{-1}): 3068; 2951; 1716; 1676; 1634; 1588; 1557; 1441; 1297; 1259; 1215; 1148; 1089; 984; 785; 756; 697. ^{1}H NMR (DMSO-d_6): 3.33 (3H, s); 3.81 (3H, s); 6.21 (1H, s); 7.48 (2H, m); 7.74 (5H, m); 7.93 (1H, d, 6.0). ^{13}C NMR (DMSO-d_6): 43.0; 52.5; 112.6; 125.3; 125.5; 126.4; 126.5; 130.0; 130.1; 131.0; 132.1; 133.2; 134.5; 148.5; 151.6; 166.1; 181.6; 183.0. ^{1}H NMR ($CDCl_3$): 8.07 (1H, d, 8), 7.93 (1H, d, 8), 7.85 (1H, d, 8), 7.77 (1H, s), 7.70 (1H, t, 8), 7.60 (1H, t, 8), 7.45 (1H, t, 8), 7.30 (1H, d, 8), 6.18 (1H, s), 3.90 (3H, s), 3.39 (3H, s). ^{13}C NMR ($CDCl_3$): 183.8; 181.9; 166.4; 151.7; 148.3; 134.1; 132.7; 132.6; 132.4; 131.9; 129.8; 129.7; 127.4; 126.9; 126.3; 125.8; 112.9; 52.4; 43.2.

7o *N-Methyl-2-(4-fluorophenyl)amino-1,4-naphthoquinone.* Reaction time 82 h, Brown red crystals, 90% yield. M.p.: 310−311 °C; IR (cm^{-1}): 3051; 1674; 1629; 1591; 1556; 1506; 1290; 1265; 1213; 1133; 835; 779; 731; 717; 563; 534. HRMS (*m*/*z*): Obs. 282.0920; Calcd 282.0930 ($C_{17}H_{13}FNO_2^+$). ^{1}H NMR (DMSO-d_6): 3.29 (3H, s); 6.11 (1H, s); 7.21 (4H, m); 7.76 (3H, m); 7.93 (1H, d, 6.0). ^{13}C NMR (DMSO-d_6): 43.4; 111.4; 116.2 (d, $^{2}J_{CF}$ 22.5); 125.2; 126.5; 127.3 (d, $^{3}J_{CF}$ 8.5); 132.2; 132.3; 133.2; 134.5; 144.5 ($^{4}J_{CF}$ 1.5); 152.0; 181.8; 182.9; δ C−F not observed. ^{1}H NMR ($CDCl_3$): 8.05 (1H, d, 8), 7.87 (1H, d, 8), 7.69 (1H, t, 8), 7.59 (1H, t, 8), 7.07 (4H, m), 6.09 (1H, s), 3.36 (3H, s). ^{13}C NMR ($CDCl_3$): 183.7; 182.2; 161.0 (d, $^{1}J_{CF}$ 245); 151.9; 144.1 ($^{4}J_{CF}$ 3.5); 134.1; 132.6; 132.5; 127.0 (d, $^{3}J_{CF}$ 8.5); 126.8; 125.7; 116.6 (d, $^{2}J_{CF}$ 22.5); 111.9; 43.5.

7p *N-Methyl-2-(4-chlorophenyl)amino-1,4-naphthoquinone*[43]. Reaction time 24 h, Brown red crystals, 58% yield. M.p.: 142−144 °C. IR (cm^{-1}): 3055; 1677; 1629; 1592; 1560; 1488; 1297; 1137; 1089; 1064; 842; 785; 731; 715; 557. HRMS (*m*/*z*): Obs. 298.0624; Calcd 298.0635 ($C_{17}H_{13}ClNO_2^+$). ^{1}H NMR (DMSO-d_6): 3.31 (3H, s); 6.22 (1H, s); 7.23 (2H, d, 8.0); 7.39 (2H, d, 8.0); 7.78 (3H, m); 7.95 (1H, d, 6.0). ^{13}C NMR: 42.8; 112.5; 125.0; 126.3; 126.7; 129.1; 129.6; 132.0; 132.1; 132.9; 134.2; 147.0; 151.5; 181.4; 182.7.

7q *N-Methyl-2-(4-bromophenyl)amino-1,4-naphthoquinone*[43]. Reaction time 79 h, Burgundy crystals, 60% yield. M.p.: 154−156 °C; IR (cm^{-1}): 3051; 1678; 1629; 1593; 1560; 1486; 1295; 1263; 1137; 785; 729; HRMS (*m*/*z*): Obs. 342.0118; Calcd 342.0130 ($C_{17}H_{13}BrNO_2^+$). ^{1}H NMR (DMSO-d_6): 3.29 (3H, s); 6.21 (1H, s); 7.15 (2H, d, 8.0); 7.50 (2H, d, 10.0); 7.76 (3H, m); 7.93 (1H, d; 6.0). ^{13}C NMR: 42.8; 112.7; 117.9; 125.2; 126.5; 127.2; 132.1; 132.1; 132.2; 133.1; 134.4; 147.5; 151.6; 181.5; 182.8. ^{1}H NMR ($CDCl_3$): 8.06 (1H, d, 6), 7.87 (1H, d, 8), 7.70 (1H, t, 6), 7.60 (1H, t, 8), 7.48 (2H, d, 8), 6.98 (2H, d, 8), 6.16 (1H, s), 3.35 (3H, s). ^{13}C NMR ($CDCl_3$): 183.8; 182.0; 151.7; 147.2; 134.2; 132.8; 132.8; 132.6; 132.4; 126.9; 125.8; 119.7; 112.9; 43.1.

7s *N-Methyl-2-(3-chloro-4-methoxyphenyl)amino-1,4-naphthoquinone.* Reaction time 79 h, Burgundy crystals, 73% yield. M.p.: 143−144 °C; IR (cm^{-1}): 3053; 2964; 1674; 1626; 1595; 1560; 1504; 1294; 1253; 1139; 1062; 1022; 962; 783; 725; 613. HRMS (*m*/*z*): Obs. 328.0730; Calcd 328.0741 ($C_{18}H_{15}ClNO_3^+$). ^{1}H NMR (DMSO-d_6): 3.29 (3H, s); 3.87 (3H, s); 6.11 (1H, s); 7.09 (1H, d, 8); 7.17 (1H, dd, 8, 2); 7.39 (1H, d, 2.0); 7.76 (3H, m); 7.93 (1H, m). ^{13}C NMR: 43.1; 56.2; 111.1; 112.9; 121.1; 124.9; 125.1; 126.2; 126.7; 132.0; 132.7; 134.1; 141.3; 151.5; 152.5; 181.5; 182.4.

7u *N-Methyl-2-(2-methoxy-4-nitrophenyl)amino-1,4-naphthoquinone.* Reaction time 20 h, Bright red crystals, 68% yield. M.p.: 128−130 °C; IR (cm^{-1}): 3078; 1678; 1628; 1594; 1557; 1517; 1500; 1340; 1293; 1267; 1256; 1126; 1088; 1028; 870; 806; 775; 723. ^{1}H NMR (DMSO-d_6): 3.30 (3H, s); 3.71 (3H, s); 6.20 (1H, s); 7.51 (1H, d, 8.0); 7.83 (6H, m). ^{13}C NMR (DMSO-d_6): 41.7; 56.6; 107.3; 109.8; 117.1; 125.3; 126.3; 126.3; 131.7; 132.1; 133.2; 134.5; 143.2; 145.3; 151.9; 153.0; 180.8; 183.0. ^{1}H NMR ($CDCl_3$): 8.08 (1H, d, 8), 7.90 (1H, dd, 8, 2), 7.84 (1H, d, 8), 7.77 (1H, d, 2), 7.71 (1H, t, 8), 7.61 (1H, t, 8), 7.24 (1H, d, 8), 6.16 (1H, s), 3.80 (3H, s). ^{13}C NMR ($CDCl_3$): 184.0; 181.3; 153.9; 151.7; 146.3; 143.2; 134.2; 132.8; 132.7; 132.0; 126.6; 126.2; 125.9; 117.3; 110.8; 107.4; 56.4; 41.9.

■ ASSOCIATED CONTENT

Supporting Information. Complete nongeneralized experimental parameters and copies of the spectra from which the reported spectroscopic data were obtained. This material is available free of charge via the Internet at http://pubs.acs.org.

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